Primary Immunodeficiency in Adults

ALTHOUGH MANY of the syndromes associated with primary immunodeficient states were described in infants and children, it has become increasingly evident that immunodeficiencies not secondary to other diseases occur also in adults. Most of these patients have either a selective IgA deficiency (<0.05 mg per ml of serum) or a more global deficiency. The latter are placed under the heading "common variable immunodeficiency," defined by a World Health Organization classification committee in 1971 as a heterogeneous group of disorders characterized by hypogammaglobulinemia and susceptibility to infections but variable with respect to age of onset, patterns of clinical manisfestations and presence of cellular immune dysfunction. Although the immunoglobulins are produced by plasma cells derived from B (bursal equivalent) lymphocytes, most of the patients are not deficient in these cells. The defect appears to be in secretion of immunoglobulins. T suppressor cells, decreased T helper activity, a serum inhibitory factor and a missing serum factor have been detected in various patients.

The clinical presentation may be more similar than different in both groups. Sinopulmonary disease is common, a result of recurring infections with common pyogenic organisms leading to chronic sinusitis, recurring pneumonias and to peripheral bronchiectasis. Some patients develop a sprue-like illness and autoimmune diseases such as systemic lupus erythematosus and pernicious anemia. Food and drug reactions are relatively frequent.

Patients with common variable immunodeficiency usually have more serious pulmonary disease than those with only IgA deficiency, and they have a propensity for neoplasia. In one series, 16 percent developed malignancies, three fourths of which were of the epithelial type and the remaining lymphoreticular. Since many of these manifestations have in the past been considered evidence of immunological excess and treated with immunosuppressive agents, this viewpoint needs to be reassessed in light of the findings in primary immunodeficiency in adults.

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Reactions to Food Additives

IN 1959 Lockey reported the cases of three patients who developed urticaria from tartrazine yellow, an azo dye in their steroid medications. He noted that the same dye is used also for coloring foods, wool and silk. In the past 20 years additional reports have appeared implicating tartrazine yellow as a cause of urticaria, angioedema, asthma, or occasionally a violent systemic reaction. Although many of the reported cases have not been thoroughly documented, a large number of the tartrazine-reactive patients have a history of aspirin sensitivity and nasal polyps.

In 1969 Chaffee and Settipane reported the case of a patient with attacks of asthma and angioedema from the food preservative sodium benzoate, as well as from aspirin and tartrazine. Juhlin and co-workers did provocative oral challenges on eight patients with aspirin-sensitive asthma and found that seven reacted to tartrazine and two to sodium benzoate, and of 52 patients with chronic recurrent urticaria 35 developed hives after challenge with aspirin, 19 reacted to tartrazine and 22 to sodium benzoate. Other investigators have reported a considerably lower prevalence of reactors to these chemicals. Stenius and Lemola found that 25 of 140 asthmatic patients had a positive bronchoconstrictor response to challenge with tartrazine, although only 9 of these gave a history of aggravation of their asthma after ingestion of foods and drugs known to contain tartrazine, and another 7 patients with such a history gave a negative response to deliberate challenge.

Recently Freedman has added sulfur dioxide, a preservative used in orange drinks, to the list of additives causing asthma. This compound, which for years has been known to aggravate asthma when inhaled, caused bronchial constriction within two minutes when given by ingestion, and the effect was blocked by cromolyn sodium.

The mechanism by which these chemical additives cause asthma or urticaria is unknown. There is no evidence that immunologic hypersensitivity is involved, and because of the strong association with aspirin sensitivity it is probable that a nonimmunologic mechanism is involved in reactions to aspirin and the food additives. Several possible modes of pharmacologic idiosyncrasy have been proposed to account for aspirin-sensitive asthma. At present the prevailing theory of aspirin sensitivity is based on the known ability of aspirin

to inhibit the biosynthesis of prostaglandins. Preferential inhibition of prostaglandin E synthesis in the lung, permitting the action of prostaglandin $F_{2\alpha}$, a potent bronchoconstrictor, to remain unopposed, would explain the asthmatic response. The mechanism underlying urticaria and angioedema provoked by aspirin could be a different one, although the role of prostaglandins has not been excluded. In many patients with chronic urticaria, aspirin seems to act as a nonspecific potentiator. The results of experiments to study the effect of tartrazine, benzoates and sulfur dioxide on prostaglandin biosynthesis will be eagerly awaited.

Feingold has proposed that many unspecified food additives and "natural salicylates" may cause hyperactivity and learning disabilities in some children. This theory has gained popular support, but several recent controlled studies of his additive- and salicylate-free diet have shown equivocal or no improvement in children with these disorders.

Food additives, numbering in the thousands, are widely employed to alter the color, taste, and texture of the food and to preserve freshness and inhibit contamination. It is therefore not surprising that some patients may exhibit idiosyncrasy or allergy to one or more of these substances.

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The Use of Antihistamines in Bronchial Asthma

ANTIHISTAMINES have been considered to provide either no benefit or even to be contraindicated in all asthmatic patients. However, recent studies have shown that these drugs do not necessarily cause a deterioration of the asthmatic state, and in fact may provide benefit. Antihistamines not only block H_1 receptors and thus partially block allergen induced bronchospasm, but they appear to have an anticholinergic effect as well. Popa has reported that high doses of chlorpheniramine given intravenously result in a significant degree of bronchodilation in asthmatic patients without atropine-like side effects. Furthermore, Karlin and co-workers have shown improved pulmonary function in patients with mild asthma receiving twice the usual recommended dosage. No adverse effects were seen in patients with chronic severe asthma receiving antihistamines for coexisting allergic rhinitis or urticaria.

These recent studies warrant the following conclusions:

- Asthmatic patients with allergic rhinitis may safely receive antihistamines in the usual dosage, and there is no evidence that coexisting asthma will be exacerbated.
- Although antihistamines can improve asthma in some cases, their use in asthmatic patients must be established on an individual basis.
- The use of antihistamines in patients with status asthmaticus cannot be recommended at this time because of the existence of more effective drugs and because potential drying effect of antihistamines on bronchial mucus has not been firmly clarified.

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The Measurement of IgE

THE AMERICAN ACADEMY OF ALLERGY has appointed a Committee on Standardization of In Vitro Tests which is charged with defining and correcting the problems in the quantitation of IgE. They conducted a nationwide single-blind evaluation of the accuracy and reproducibility of the quantitation of IgE which showed an unacceptable level of variation. Besides the large variation between laboratories, the variation of repeated assays within laboratories was unacceptably large.

Part of the problem is undoubtedly due to differences in assay methods. A study of the various assay methods—radioimmunosorbent test (RIST), double-antibody radioimmunoassay (RIA), radial immunodiffusion (RID) and paper disc immunosorbent test (PRIST)—shows that RIST and RID may lead to spurious elevations of IgE in sera and secretions. Double-antibody RIA and PRIST provide the best agreement, but PRIST may give deceptively low results in certain sera. When all 14 laboratories assayed the test serum with the PRIST kit, variations within and between laboratories (133 units per ml to 330 units per ml) were still more than 2½ fold. The problems of the quantitation of IgE are being resolved and a "predictive" table of serum IgE levels in infants,